UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/693,307	10/24/2003	Shalaby W. Shalaby	PC25466A	1484

23913 7590 09/28/2007

PFIZER INC
Steve T. Zelson
150 EAST 42ND STREET
5TH FLOOR - STOP 49
NEW YORK, NY 10017-5612

EXAMINER	
MAEWALL, SNIGDHA	

ART UNIT	PAPER NUMBER
1615	

MAIL DATE	DELIVERY MODE
09/28/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/693,307	SHALABY ET AL.	
	Examiner	Art Unit	
	Snigdha Maewall	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *07/11/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Receipt of Applicant's Arguments and IDS filed on 07/11/02007 is acknowledged. Claims pending in the prosecution are **1-13.**

The rejection made under 35 USC 112.2 in the Office action dated 02/12/2007 is hereby withdrawn in view of Applicant's Arguments.

The following rejections of record are maintained.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a written description rejection.** Instant claims are generic with respect to 'bioactive agent" and have not been sufficiently described to show possession of compositions comprising the entire genus. The invention defined by the claims requires a specific type physiochemical interaction between the bioactive agent and a polymer in order to produce the desired result. With

regard to the bioactive agent, the aryl- heterocyclic compounds described in US 4,831,031 (incorporated by reference into instant disclosure on page 3 of the specification) are sufficiently similar in structure or function that the showing of ziprasidone is sufficient to show possession of this sub- genus. However, this showing is not sufficient to show possession of all bioactive agents, or all aryl-heterocyclic compounds. The genus of bioactive agent, and the sub-genus of aryl-heterocyclic compound, includes materials having disparate functions and properties. These materials may be hydrophilic or hydrophobic; they may be anionic, cationic, zwitterionic, or neutral; they may have one or more of a multitude of biological functions. Clearly, the showing in the specification, which is limited to ziprasidone, is not sufficient to show possession of all such materials in the context of the invention.

Response to Arguments

4. Applicant's arguments filed on 07/11/2007 have been fully considered but they are not persuasive.

Applicant argues that the "specification indicates that basic, e.g. amine groups, or acidic, e.g. carboxyl groups, can provide suitable ionic attraction to generate ionic bonding whereby the conjugates of the invention form (see page 3, lines 3-6; and page 4, lines 31-34). Hence, Applicants maintain that the subject application provides adequate written description of the genus "bioactive agents" for purposes of its relevance to the claimed invention." In response to this argument , Examiner points out

that the disclosure of ionic bonding in order to make ionic conjugates between only one bioactive agent such as ziprasidone and liquid polymer is not enough to show possession of any or every bioactive agent or aryl heterocyclic compound which would form ionic conjugate with the claimed polymer. Further, in the absence of specific structural limitations present with respect to the bioactive compound, it is the position of the Examiner that structural and functional relationship cannot be deduced. Hence the rejection n is maintained.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-5, 7-8, 11 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Shalaby to (U.S. Patent No. 5,714,159).

Shalaby discloses a hydrogel-forming, self-solvating, absorbable polyester copolymers capable of selective, segmental association into a compliant hydrogel mass on contact with an aqueous environment (abstract). According to Shalaby, the copolymer comprises a base component, designated as "Component A". The "Component A" refers to the basic structure of the copolymers of the invention. "Component A" comprises a molecular chain having

a hydrophilic block "Y" and a relatively hydrophobic polyester block "X" . The hydrophobic block/segmented polymer comprises a polyester formed by grafting a glycolide, lactide, .epsilon.-caprolactone, p-dioxanone, trimethylene carbonate or combinations thereof, onto the hydroxylic or amino groups of a hydrophilic polymer precursor. The hydrophilic block comprises a polyoxyethylene, poly(oxyethylene-b-oxypropylene), polypeptide polyalkylene oxamate, a polysaccharide, and derivatives thereof; or a liquid, high molecular weight polyether glycol interlinked with an oxalate or succinate functionalities in linear or branched form (column 6 and 7, lines 65-67 and 1-15).
"Component A" optionally comprises carboxylic end groups which facilitates ionically binding a bioactive agent or drug (column 7, lines 19-23). The composition comprises an absorbable carrier which helps in immediate and controlled release of the bioactive drug.(column 7, lines, 30-33).

According to Shalaby a copolymer optionally comprises a bioactive agent, such a copolymer is capable of the controlled-release of a biologically active agent for modulating cellular events such as wound healing and tissue regeneration (column 6, lines 30-45). The copolymer described by Shalaby is capable of being injected into living tissues (column 6, line 57) (hence proving that the copolymer is liquid conjugate). The hydrophobic block "X" as described above refers to absorbable polyester chain block(s) or segment(s) of variable length, which is a viscous liquid at room temperature.

These hydrophobic block (s) "X "comprises, copolymeric segments of glycolide, l-lactide, trimethylene carbonate (column 8, lines 4-9).

The "Hydrophilic Block(s)" or segment (s) "Y", comprises poly(oxyethylene) (column 8, lines 17-18).

Shalaby further discloses that the length of the hydrophilic block "Y" and its weight fractions can be varied to modulate the rate of gel formation, its modulus, its water content, and diffusivity of bioactive drug (column 8, lines 23-37). Shalaby discloses that to render "Component A" more receptive to basic drugs, its end-groups can optionally be carboxylated (column 10, lines 1-5). "Component A" can be succinylated to provide acidic end-groups for ionic binding on the bioactive agent/drug (column 12, lines 8-10). Shalaby further discloses that liquid compositions made of component A with or without drug or bioactive agent can form hydrogels upon contacting a liquid environment (column 12, lines 10-12). The "Component A" as disclosed in the reference, comprises an inherent viscosity at 25 degrees C in chloroform ranging between 0.03 to 0.80 dL/g and can be present as a liquid at room temperature and can be administered through a syringe needle (column 10, lines 10-17). The liquid conjugate, "Component A" in this case can combine with bioactive drugs such as calcium (column 12, lines 58-59) hence proving the ionic bond linkage between the liquid conjugate and the bioactive drug.

Response to Arguments

7. Applicant's arguments filed 07/11/2007 have been fully considered but they are not persuasive. Applicant argues "..... that the Shalaby reference (US 5,714,159)

fails to disclose "a liquid conjugate" as claimed in the subject application, and therefore, also fails to disclose a liquid conjugate comprising a bioactive agent at least partially ionically bonded to an absorbable liquid polymer..". Applicant's arguments are mainly to prove that the prior art (US 5,714,159) does not teach liquid conjugate as claimed in the instant application. In response to the Applicant's extensive arguments, Examiner points to Column 13, lines 58-65 and column 14, lines 1-5 where it is stated that in one of the embodiments, the pharmaceutical formulation comprises an injectable viscous fluid of Component A, Components A/B, Components A/B/C and /or Components A/C. Example V on column 18 depicts liquid formulations, describing injectable formulations. On column 9, lines 57-59, the prior art discloses that a liquid, high molecular weight polyether glycol interlinked with oxalate or succinate functionalities can be utilized in the formulation of the polymer. Furthermore, on column 10, lines 10-15, Shalaby discloses that Component A of the invention comprises an inherent viscosity at 25 degrees C in chloroform ranging between 0.03 to 0.80 dL/g and can be present as a liquid at room temperature and can be administered through a syringe needle (column 10, lines 10-17). Shalaby also discloses that the claimed polymers are useful in for prolonged and controlled dispersing of range of drugs such as calcium (see column 12, lines 58-60). Based on the foregoing disclosure it is evident/inherent that the claimed polymer is liquid in nature and due to the presence of carboxylic function, the polymer forms an ionic interaction with the bioactive agent which are basic in nature. Since the polymer comprises carboxylic group, it is the position of the examiner that one skilled in the art

would expect and ionic conjugation with the basic drugs, hence the rejection of record is maintained.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1-3, 6, 9-10 and 12-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shalaby to (U.S. Patent No. 5,714,159) in view of Kim et al. to (U.S. Patent No. 6,232,304 B1).

Teachings of Shalaby have been discussed above.

Shalaby to (U.S. Patent No. 5,714,159) does not specifically teach the bioactive agent such as Ziprasidone (aryl- heterocyclic compound).

Kim et al. teaches aryl- heterocyclic drug such as Ziprasidone. Kim et al. discloses that increasing drug solubility and stability through appropriate formulation can lead to therapeutic efficacy of the drug (column 1, lines 17-20). On (column 3, lines 10-27), Kim et al. discloses that ziprasidone has utility as a neruleptic drug, and is thus useful as neuroleptic/antipsychotic drug (column 3, lines 26-30). Since the object of both Shalaby and Kim et al. is to increase the drug solubility, it would have been obvious to

one of ordinary skilled in the art at the time the invention was made to utilize Ziprasidone in the liquid conjugate as a bioactive drug or alternately to use polymers and carboxyl-bearing polymers or carboxyl-bearing block/segment as forwarded by Shalaby, with Ziprasidone to make liquid conjugate because Ziprasidone acts as an antipsychotic as disclosed my Kim et al. Addionally, since Ziprasidone happens to be basic in nature, it would be expected for ziprasidone to form ionic bond with carboxyl-bearing polymers or block/ segment copolymers which are acidic in nature. A skilled artisan would thus have been motivated to formulate a liquid conjugate comprising Ziprasidone and absorbable polymer with one or more carboxyl group with a reasonable expectation of success.

Response to Arguments

10. Applicant's arguments filed 07/11/2007 have been fully considered but they are not persuasive.

Applicant Argues that "Kim et al. does not specify the use of the ionic conjugation approach nor direct the attention of one ordinarily skilled in the art to a polymer as described in the present application." In response to this argument, it is stated that the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). In the instant case, due to the basic characteristics of Ziprasidone and the claimed

polymer, a skilled artisan would have expected to form ionic conjugated product with a reasonable expectation of success. Shalaby's reference teaches ionic conjugate such as polymers with carboxyl groups and suggests being used with basic active agents. Ziprasidone comprises nitrogen with lone pair of electron; therefore, a skilled artisan would have formulated a liquid conjugated product with an expectation of the product comprising ionic conjugation due to acidic and basic characteristics with a reasonable expectation of success.

11. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Snigdha Maewall whose telephone number is (571)-

272-6197. The examiner can normally be reached on Monday -Friday from 8:30 A.M to 5:00 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gollamudi S. Kishore, PhD
Primary Examiner
Group 1600

Snigdha Maewall

Art Unit 1615